FLUORESCENCE OPTICAL TUMOR IMAGING (FOTI)

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The early stages of tumor progression and micrometastasis formation have been difficult to image and visualize due to the inability to identify small numbers of tumor cells against a background of host tissue. The imaging and visualization of tumor invasion and micrometastasis formation in live animals can be a major factor in understanding tumor progression and its control. To enhance the resolution of imaging and visualization of micrometastases and metastases in fresh tissue and the live animal, we have stably transfected the green fluorescent protein (GFP) gene, cloned from the bioluminescent jellyfish *Aequorea victoria* into human and rodent cancer cells (*Cancer Res.*, 57:2042-2047, 1995; *Clin Exp Meta* 15:547-552, 1997; *Anticancer Res* 17:2377-2384, 1997; *In Vitro Cell Dev Biol* 33:745-747, 1997; *PNAS*, 94:11573-11576, 1997). The stable GFP transfectants are highly fluorescent *in vivo* in tumors in orthotopic-transplant rodent models which allow spontaneous metastasis. Recently we have developed bone metastasis model of lung cancer (*Cancer Res* 58:4217-4221, 1998) and prostate (*Cancer Res.,* 58:4217-4221, 1998). The high-level GFP expression enables the real-time fluorescence optical tumor imaging (FOTI) and visualization of the primary tumor and regional and distant metastases in their normal target organs such as brain, bone, lymph node, and liver in live animals. A Princeton Instrument CCD thermo-electrically-cooled camera is used to collect the optical images from a fluorescence Leica dissecting microscope with a mercury lamp which are analyzed and processed with Image Pro-Plus software. We have now developed fluorescent nude mouse models of specific organ metastasis including bone, liver, brain, and lymph nodes in which the tumor can be followed externally in the intact animals by FOTI. We have isolated for external FOTI, 25 GFP-expressing human cancer cell lines including melanoma, colon, lung, breast, and prostate cells that stably express GFP *in vitro* and *in vivo*. We are determining the organs involved with tumor and metastases that are most optimally imaged in intact animals by GFP expression.